## SEQUENCE LISTING

2110 M 1 71 N N N N N
<110> Chambon, Pierre - Metzger, Daniel
<120> Transgenic mouse for targeted recombination mediated by modified Cre-ER
<130> D18961
<150> FR 00 12 570 <151> 2000-10-03
<160> 14
<170> PatentIn Ver. 2.1
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ato one otg gag ogg occ otg ggo gag gtg tac otg gac agc agc aag 144 Ilo Pro Leu Glu Arg Pro Leu Gly Glu Val Tyr Leu Asp Ser Ser Lys 35 40 45
cee gee gtg tae aac tae eee gag gge gee gee tae gag tte aac gee 192 Pro Ala Val Tyr Asn Tyr Pro Glu Gly Ala Ala Tyr Glu Phe Asn Ala 50 55 60
geg gee gee aac geg cag gte tac ggt cag acc ggc etc eec tac 240 Ala Ala Ala Asn Ala Gln Val Tyr Gly Gln Thr Gly Leu Pro Tyr 65 70 75 80
ggc cee ggg tet gag get geg tte ggc tee aac ggc etg ggg ggt 200 Gly Pro Gly Ser Glu Ala Ala Ala Phe Gly Ser Asn Gly Leu Gly Gly 85 90 · 95
ttc ccc cca etc aac age gtg tct ccg age eeg ctg atg cta ctg cac 336 Phe Pro Pro Leu Asn Ser Val Ser Pro Ser Pro Leu Met Leu Leu His 100 105 110
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ccc tac tac ctg gag aac gag ccc agc ggc tac acg gtg cgc gag gcc 432 Pro Tyr Tyr Leu Glu Asn Glu Pro Ser Gly Tyr Thr Val Arg Glu Ala 130 135 140

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	_	_	aga Arg	_	_	-			_	_		_	_	•	-	528
			aag Lys 180													576
			cat His													624
	_	•	agt Ser						-		_	_		-		672
	_	-	acc Thr		-					_			_	_	_	720
		-	aaa Lys	_		-			_	•					-	768
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			ggc Gly													864
			tgg Trp		_			_			_		-	_		912
	_	_	ttg Leu		-	_	-	-	-	_	_	_	-	-		960
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			gct Ala 340													1056
			cac His													1104
			ctc Leu													1152
gag	atc	ctg	atg	att	ggt	ctc	gtc	tgg	cgc	tcc	atg	gag	cac	cca	aaa	1200

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<213> Homo sapiens

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Asp Gly Glu Gly Arg Gly Glu Val Gly Ser Ala Gly Asp Mct Arg Ala Asp Ala Asp Leu Trp Pro Ser Pro Leu Met Ile Lys Arg Ser Lys Lys Asp Ser Leu Ala Leu Ser Leu Thr Ala Asp Gln Met Val Ser Ala Leu Leu 305

Asp Ala Glu Pro Pro Ile Leu Tyr Ser Glu Tyr Asp Pro Thr Arg Pro 325 330 335

Fhe Ser Glu Ala Ser Met Met Gly Leu Leu Thr Asn Leu Ala Asp Arg 340 345 350

Glu Leu Val His Met Ile Asn Trp Ala Lys Arg Val Pro Gly Phe Val 355 360 365

Asp Leu Thr Leu His Asp Gln Val His Leu Leu Glu Cys Ala Trp Leu 370 375 380

Glu Ile Leu Met Ile Gly Leu Val Trp Arg Sar Met Glu His Pro Gly 385 390 395 400

Lys Leu Leu Phe Ala Pro Asn Leu Leu Leu Asp Arg Asn Gln Gly Lys
405
410
415

Cys Val Glu Gly Met Val Glu Ile Phe Asp Met Leu Leu Ala Thr Ser
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Ser Arg Phe Arg Met Met Asn Leu Gln Gly Glu Glu Phe Val Cys Leu 435 440 445

Lys Ser Ile Ile Leu Leu Asn Ser Gly Val Tyr Thr Phe Leu Ser Ser 450 460

Thr Leu Lys Ser Leu Glu Glu Lys Asp His Ile His Arg Val Leu Asp 465 470 475 480

Lys Ile Thr Asp Thr Leu Ile His Leu Met Ala Lys Ala Gly Leu Thr 485 490 495

Leu Gln Gln His Gln Arg Leu Ala Gln Leu Leu Leu Ile Leu Ser 500 505 510

His Ile Arg His Met Ser Asn Lys Gly Met Glu His Leu Tyr Ser Met 515 520 525

Lys Cys Lys Asn Val Val Pro Leu Tyr Asp Leu Leu Leu Glu Met Leu 530 540

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<211> 1983

<212> DNA

<213> Artificial sequence

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Val	Glu 210	Lys	, Ala	Leu	Ser	Leu 215	Gly	Val	Thr	Lys	Leu 220		Glu	Arg	Trp	
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					ggt Gly											768
					qaa Glu								_	_		816
					gac Asp											864
					gga Gly		Ala									912
tca Ser 305	ata Ilc	ccg Pro	gag <b>G</b> lu	at¢ Ile	atg Met 310	caa Gln	gct Ala	ggt Gly	ggc Gly	tgg Trp 315	acc Thr	aat Asn	gta Val	aat Asn	att Ile 320	960
					cgt Arg											1008
_	-	_		_	ggc Gly	-					-		_		-	1056
					çça Pro											1104
					tcc Ser											1152
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ccc Pro	ttc Phe	agt Ser	gaa Glu	gct Ala 405	tcg Ser	atg Met	atg Met	ggc Gly	tta Leu 410	ctg Leu	acc Thr	aac Asn	ctg Leu	gca Ala 415	gac Asp	1248
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					_				gtg Val				_		1584
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									atg Met 555						1680
									cag Gln						1728
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_	_	-	-		_				gac Asp		_	_	_ •-	-	1824
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<213> Artificial sequence

<223> Chimeric sequence Homosapiens-Bacteriophage P1

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Ser Ile Pro Glu Ile Met Gln Ala Gly Gly Trp Thr Asn Val Asn Ile

Val Met Asn	Tyr Ile	Arg Asn	Leu Asp	Ser Gl	lu Thr	Gly A	la Met	Val
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- Ala Ala Asn Leu Trp Pro Ser Pro Leu Met Ile Lys Arg Ser Lys Lys 355 360 365
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- Leu Asp Ala Glu Pro Pro Ile Leu Tyr Ser Glu Tyr Asp Pro Thr Arg 385 390 395 400
- Pro Phe Ser Glu Ala Ser Met Met Gly Leu Leu Thr Asn Leu Ala Asp 405 410 415
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- Val Asp Leu Thr Leu His Asp Gln Val His Leu Leu Glu Cys Ala Trp
  435 440 445
- Leu Glu Ile Leu Met Ile Gly Leu Val Trp Arg Ser Met Glu His Pro 450 455 460
- Gly Lys Leu Leu Phe Ala Pro Asn Leu Leu Leu Asp Arg Asn Gln Gly 465 470 475
- Lys Cys Val Glu Gly Met Val Glu Ile Phe Asp Met Leu Leu Ala Thr \$485\$
- Ser Ser Arg Phe Arg Met Met Asn Leu Gln Gly Glu Glu Phe Val Cys 500 505 510
- Leu Lys Ser Ile Ile Leu Leu Asn Ser GLy Val Tyr Thr Phe Leu Ser 515 520 525
- Ser Thr Leu Lys Ser Leu Glu Glu Lys Asp His Ile His Arg Val Leu 530 535 540
- Asp Lys Ile Thr Asp Thr Leu Ile His Leu Met Ala Lys Ala Gly Leu 545 550 555 560
- Thr Leu Gln Gln His Gln Arg Leu Ala Gln Leu Leu Ile Leu 565 570 575
- Ser His Ile Arg His Met Ser Asn Lys Arg Met Glu His Leu Tyr Ser 580 585 590
- Met Lys Cys Lys Asn Val Val fro Leu Tyr Asp Leu Leu Glu Met 595 600 605
- Leu Asp Ala His Arg Leu His Ala Pro Thr Ser Arg Gly Gly Ala Ser 610 620
- Val Glu Glu Thr Asp Gln Ser His Leu Ala Thr Ala Gly Ser Thr Ser 625 630 635 640
- Ser His Ser Leu Gln Lys Tyr Tyr Ile Thr Gly Glu Ala Glu Gly Phe

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Pro Ala Thr Val 660

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ctg gca ttt ctg ggg att gct tat aac acc ctg tta cgt ata gcc gaa

	Leu	Ala	Phe	Leu	Gly 165	Ile	Ala	Tyr	Asn	Thr 170	Leu	Leu	Arg	Ile	Ala 175	Glu	
		_			agg Arg	_		_			_					-	576
					att Ile												624
	-		_	-	ctt Leu	_	-		_			_	-		-		672
					ggt Gly												720
		-	_		aat Asn 245	~ -	_	-						_	-		768
					ctg Leu												916
			_	-	gat Asp	_			_	-		_	_				864
					gtc Val												91,2
					atc Ile												960
					atc Ile 325												1008
	cgc Arg	ctg Leu	ctg Leu	gaa Glu 340	gat Asp	Gl <b>y</b> ggc	gat Asp	ctc Leu	gag Glu 345	cca Pro	tct Ser	gct Ala	gga Gly	gac Asp 350	atg Met	aga Arg	1056
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					ttg Leu												1152
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gtg aag cta ctg Val Lys Leu Leu : 465			
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ctc aaa tct att : Leu Lys Ser Ile : 515	<del>-</del>		<u>-</u>
age acc ctg aag : Ser Thr Leu Lys : 530			
gac aag atc aca o Asp Lys Ile Thr 2 545			
ace cty cag cag Thr Leu Gln Gln			
tcc cac atc agg ( Ser His Ile Arg 1 580	•• ••		
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Asp Ala Thr Ser Asp Glu Val Arg Lys Asn Leu Met Asp Met Phe Arg 20 25 30

Asp Arg Gln Ala Fhe Ser Glu His Thr Trp Lys Met Leu Leu Ser Val 35 40

Cys Arg Ser Trp Ala Ala Trp Cys Lys Leu Asn Asn Arg Lys Trp Phe 50 55 60

Pro Ala Glu Pro Glu Asp Val Arg Asp Tyr Leu Leu Tyr Leu Gln Ala 65 70 75 80

Arg Gly Leu Ala Val Lys Thr Ile Gln Gln His Leu Gly Gln Leu Asn 85 90 95

Met Leu His Arg Arg Ser Gly Leu Pro Arg Pro Ser Asp Ser Asn Ala 100 105 110

Val Ser Leu Val Met Arg Arg Ile Arg Lys Glu Asn Val Asp Ala Gly 115 120 125

Glu Arg Ala Lys Gln Ala Leu Ala Phe Glu Arg Thr Asp Phe Asp Gln 130 135 140

Val Arg Ser Leu Met Glu Asn Ser Asp Arg Cys Gln Asp Ile Arg Asn 145 150 155 160

Leu Ala Phe Leu Gly Ile Ala Tyr Asn Thr Leu Leu Arg Ile Ala Glu 165 170 175

Ile Ala Arg Ile Arg Val Lys Asp Ile Ser Arg Thr Asp Gly Gly Arg 180 185 190

Met Leu Ile His Ile Gly Arg Thr Lys Thr Leu Val Ser Thr Ala Gly 195 200 205

Val Glu Lys Ala Leu Ser Leu Gly Val Thr Lys Leu Val Glu Arg Trp 210 215 220

Ile Scr Val Ser Gly Val Ala Asp Asp Pro Asn Asn Tyr Leu Phe Cys 225 230 235 240

Arg Val Arg Lys Asn Gly Val Ala Ala Pro Ser Ala Thr Ser Gln Leu 245 250 255

Ser Thr Arg Ala Leu Glu Gly Ile Phe Glu Ala Thr His Arg Leu Ile Tyr Gly Ala Lys Asp Asp Ser Gly Gln Arg Tyr Leu Ala Trp Ser Gly His Ser Ala Arg Val Gly Ala Ala Arg Asp Met Ala Arg Ala Gly Val Ser Ile Pro Glu Ile Met Gln Ala Gly Gly Trp Thr Asn Val Asn Ile Val Met Asn Tyr Ile Arg Asn Leu Asp Ser Glu Thr Gly Ala Met Val 330 325 Arg Leu Leu Glu Asp Gly Asp Leu Glu Pro Ser Ala Gly Asp Met Arg Ala Ala Asn Leu Trp Pro Ser Pro Leu Met Ile Lys Arg Ser Lys Lys Asn Ser Leu Ala Leu Ser Leu Thr Ala Asp Gln Met Val Ser Ala Leu 375 Leu Asp Ala Glu Pro Pro Ile Leu Tyr Ser Glu Tyr Asp Pro Thr Arg Pro Phe Ser Glu Ala Ser Met Met Gly Leu Leu Thr Asn Leu Ala Asp 410 Arg Glu Leu Val His Met Ile Asn Trp Ala Lys Arg Val Fro Gly Phe Val Asp Leu Thr Leu His Asp Gln Val His Leu Leu Glu Cys Ala Trp Leu Glu Ile Leu Met Ile Gly Leu Val Trp Arg Ser Met Glu His Pro Val Lys Leu Leu Phe Ala Pro Asn Leu Leu Asp Arg Asn Gln Gly Lys Cys Val Glu Gly Met Val Glu Ile Phe Asp Met Leu Leu Ala Thr 490 Ser Ser Arg Phe Arg Met Met Asn Leu Gln Gly Glu Glu Phe Val Cys Leu Lys Ser Ile Ile Leu Leu Asn Ser Gly Val Tyr Thr Phc Leu Ser 520 Ser Thr Leu Lys Ser Leu Glu Glu Lys Asp His Ile His Arg Val Leu Asp Lys Ile Thr Asp Thr Leu Ile His Leu Met Ala Lys Ala Gly Leu 550 Thr Leu Gln Gln Gln His Gln Arg Leu Ala Gln Leu Leu Leu Ile Leu

Ser His Ile Ary His Met Ser Asn Lys Gly Met Glu His Leu Tyr Ser

 Met
 Lys
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 Asn
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 Tyr
 Asp
 Leu
 Leu
 Glu
 Ala

 Ala
 Asp
 Ala
 His
 Ala
 Pro
 Thr
 Ser
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 Ala
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 Val
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 Thr
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 Gln
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<220> <223> Chimeric sequence Homosapiens-Bacteriophage Fl

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gat ege eag geg tit tet gag eat ace tgg aaa atg ett etg tee git 144 Asp Arg Gln Ala Phe Ser Glu His Thr Trp Lys Met Leu Leu Ser Val 35 40 45

tgc cgg tcg tgg gcg gca tgg tgc aag ttg aat aac cgg aaa tgg ttt 192 Cys Arg Ser Trp Ala Ala Trp Cys Lys Leu Asn Asn Arg Lys Trp Phe 50 55 60

ccc gca gaa cct gaa gat gtt cgc gat tat ctt cta tat ctt cag gcg 240 Pro Ala Glu Pro Glu Asp Val Arg Asp Tyr Leu Leu Tyr Leu Gln Ala 65 70 80

cgc ggt ctg gca gta aaa act atc cag caa cat ttg ggc cag cta aac 288
Arg Gly Leu Ala Val Lys Thr Ile Gln Gln His Leu Gly Gln Leu Ash
85
90

atg ctt cat cgt cgg tcc ggg ctg cca cga cca agt gac agc aat gct 33 Met Leu His Arg Arg Ser Gly Leu Pro Arg Pro Ser Asp Ser Asn Ala 100 105 110

gtt tca ctg gtt atg cgg cgg atc cga aaa gaa aac gtt gat gcc ggt 384

Val	Ser	Leu 115	Val	Met	Arg	Arg	Ile 120	Arg	Lys	Glu	Asn	Val 125	Asp	Ala	Gly	
	cgt Arg 130															432
	cgt Arg															480
ctg Leu	gca Ala	ttt Phe	ctg Leu	ggg Gly 165	att Ile	gct Ala	tat Tyr	aac Asn	acc Thr 170	ctg Leu	tta Leu	cgt Arg	ata Ile	gcc Ala 175	gaa Glu	528
	gçç															576
	tta Leu					Arg										624
gta Val	gag Glu 210	Lys Lys	gça Ala	ctt Leu	agc Ser	ctg Leu 215	er <sup>a</sup> aaa	gta Val	act Thr	aaa Lys	ctg Leu 220	gtc Val	gag Glu	¢ga Arg	tgg Trp	672
att Ile 225	tcc \$er	gtç Val	tet Ser	ggt Gly	gta Val 230	gct Ala	gat Asp	gat Asp	eeg Pro	aat Asn 235	aac Asn	tac Tyr	ctg Leu	ttt Phe	tgc Cys 240	720
	gtc Val															768
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	€ <b>1</b> γ															864
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	ata Ile															960
gtc Val	atg Met	aac Asn	tat Tyr	atc Ile 325	cgt Arg	aac Asn	ctg Leu	gat Asp	agt Ser 330	gaa Glu	aca Thr	<b>e</b> ∫À ààà	gca Ala	atg Met 335	gtg Val	1008
Arg	ctg Leu	ctg Leu	gaa Glu 340	gat Asp	<b>Gly</b>	gat Asp	ctc Leu	gag Glu 345	eca Pro	tct Ser	gct Ala	Gly	gac Asp 350	atg Met	aga Arg	1056
	gec Ala															1104

	355		3	60				365				
		ttg tcc Leu Ser										1152
		g ccc ccc g Pro Pro 390	Ile L					-			_	1200
		gct tcg Ala Ser 405										1240
	•	cac atg His Met										1296
, , ,	•	ctc cat Leu His	Ásp G					-	_	_		1344
		atg att Met Ile										1392
		ttt gct Phe Ala 470	Pro A									1440
_		ggc atg Gly Met 485		_		_	_	_	_	_		1488
		egc atg Arg Met	_				-					1536
		att ttg Ile Leu	Leu A									1584
age ace Ser Thr 530	ctg aag Leu Lys	tot otg Ser Leu	gaa ga Glu G 535	ag aag lu Lys	gac Asp	cat His	atc Ile 540	cac His	cga Arg	gtc Val	ctg Leu	1632
		gac act Asp Thr 550										1680
		cag cac Gln His 565										1728
		cac atg His Met										1 <b>7</b> 76
		aac gtg Asn Val	Val P									1824

			•							•						
	gac Asp 610			_						_	-			_		1872
gtg Val 625	gag Glu	gag Glu	acg Thr	gac Asp	caa Gln 630	agc Ser	cac His	ttg Leu	gcc Ala	act Thr 635	gcg Ala	ggc	tct Ser	act Thr	tca Ser 640	1920
	cat His															1968
	gcc Ala		_	tga												1983
<21 <21 <21	0> 8 1> 66 2> Pl 3> Al 3> Cl	RT :tifi			-		sapi	lens-	-Bact	eric	~	je Pl	L			
	0> 8	_	_	<b>+</b>	m) .	17.1	*** -	<b>41</b> –	3	<b>.</b>	<b>5</b>	n 1 -	Y	T1	Vn 1	
Met 1	Ser	Asn	теп	ьец 5	inr	val	nis	GIII	10	₩ĕĦ	FIO	ΑЦА	ren	15	AST	
Asp	Ala	Thr	Ser 20	Ąsp	Glu	Val	Arg	Lys 25	Asn	Leu	Met	Asp	Met 30	Phe	Arg	
двр	Arg	Gln 35	Ala	Phe	Ser	Glu	His 40	Thr	Trp	ГÄЗ	Met	Leu 45	Leu	Ser	Val	
Cys	Arg 50	Ser	Trp	Ala	Ala	Trp 55	Cās	Lys	Leu	Asn	Asn 60	Arg	Lys	Trp	Phe	
Pro 65	Ala	Glu	Pro	Glu	Asp 70	Val	Arg	Asp	Tyr	Leu 75	Leu	Tyr	Leu	Gln	Ala 80	
Arg	Gly	Leu	Ala	Val 85	Ьуз	Thr	Ile	Gln	Gln 90	His	Leu	Gly	Gln	<b>Leu</b> 95	Asn	
Met	Leu	His	Arg 100	Arg	5er	Gly	Leu	Pro 105	Arg	Pro	Ser	Asp	Ser 110	Asn	Ala	
Val	Ser	Leu 115	Val,	Met	Arg	Аrģ	Ile 120	Arg	Ļys	Glu	Asn	Val 125	Asp	Ala	Gly	
Glu	Arg 130	Ala	Ľуs	Gln	Λla	Leu 135	Ala	Phe	Glu	Arg	Thr 140	Asp	Phe	Asp	Gln	
Val 145	Arg	Ser	Leu	Met	Glu 150	Asn	Ser	Asp	Arg	Cys 155	Gln	Asp	Ile	Arg	Asn 160	
Leu	Ala	Phe	Leu	Gly 165	Ile	Ala	Tyr	Asn	Thr 170	Leu	Leu	Arg	Ile	Ala 175	Glu	
Ile	Ala	Arg	Ile 180	Arg	Val	Гйз	Asp	Ile 185	Ser	Arg	Thr	Asp	Gly 190	Gly	Arg	

Met Leu Ile His Ile Gly Arg Thr Lys Thr Leu Val Ser Thr Ala Gly Val Glu Lys Ala Leu Ser Leu Gly Val Thr Lys Leu Val Glu Arg Trp Ile Ser Val Ser Gly Val Ala Asp Asp Pro Asn Asn Tyr Leu Phe Cys Arg Val Arg Lys Asn Gly Val Ala Ala Pro Ser Ala Thr Ser Gln Leu Ser Thr Arg Ala Leu Glu Gly Ile Phe Glu Ala Thr His Arg Leu Ile 270 Tyr Gly Ala Lys Asp Asp Ser Gly Gln Arg Tyr Leu Ala Trp Ser Gly His Ser Ala Arg Val Gly Ala Ala Arg Asp Met Ala Arg Ala Gly Val Ser Ile Pro Glu Ile Met Gln Ala Gly Gly Trp Thr Asn Val Asn Ile 310 Val Met Asn Tyr Ile Arg Asn Lou Asp Ser Glu Thr Gly Ala Met Val Arg Leu Leu Glu Asp Gly Asp Leu Glu Pro Ser Ala Gly Asp Met Arg 345 Ala Ala Asn Leu Trp Pro Ser Pro Leu Met Ile Lys Arg Ser Lys Lys 360 Asn Ser Leu Ala Leu Ser Leu Thr Ala Asp Gln Met Val Ser Ala Leu Leu Asp Ala Glu Pro Pro Ile Leu Tyr Ser Glu Tyr Asp Pro Thr Arg 390 Pro Phe Ser Glu Ala Ser Met Met Gly Leu Leu Thr Asn Leu Ala Asp Arg Glu Leu Val His Met Ile Asn Trp Ala Lys Arg Val Pro Gly Phe Val Asp Leu Thr Leu His Asp Gln Val His Leu Leu Glu Cys Ala Trp Leu Glu Ile Leu Met Ile Gly Leu Val Trp Arg Ser Mat Glu His Pro Gly Lys Leu Leu Phe Ala Pro Asn Leu Leu Leu Asp Arg Asn Gln Gly Lys Cys Val Glu Gly Met Val Glu Ile Phe Asp Met Leu Leu Ala Thr 490 Ser Ser Arg Phe Arg Met Met Asn Leu Gln Gly Glu Glu Phe Val Cys

Leu Lys Ser Ile Ile Leu Leu Asn Ser Gly Val Tyr Thr Phe Leu Ser

		515	•				520					525				
Ser	Thr 530	Leu	ĽУз	Ser	Leu	Glu 535	Glu	ГЛя	Asp	His	Ile 540	His	Arg	Val	Leu	
Asp 545	Lys	Ile	Thr	Asp	Thr 550	Leu	Ile	His	Leu	Met 555	Ala	Lys	Ala	Gly	Leu 560	
Thr	Leu	Gln	Gln	Gln 565	His	Gln	Arg	Leu	Ala 570	Gln	Leu	Leu	Leu	Ile 575	Leu	
Ser	His	Ile	Arg 580	His	Met	Ser	Asn	Lys 585	Gly	Met	Glu	His	1.eu 590	Туг	Ser	
Met	Lys	Cys <b>5</b> 95	Lys	Asn	Val	Val	Pro 600	Leu	тух	Asp	Leu	Leu 605	Leu	Glu	Ala	
Ala	Asp 610	Ala	Hls	Arg	Ľeu	His 615	Ala	Pro	Thr	Ser	Arg 620	Gly	Gly	Ala	Ser	
Val 625	Glu	Glu	Thr	qeA	Cln 630	Ser	H1s	Leu	Ala	Thr 635		Gly	Ser	Thr	Ser 640	
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<211	0> 12 L> 20 2> DN	)														

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